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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,242	05/18/2005	Susumu Muto	P26130	2371

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EXAMINER	
VALENROD, YEVGENY	
ART UNIT	PAPER NUMBER
1621	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	04/09/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 04/09/2007.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/510,242	MUTO ET AL.	
	Examiner	Art Unit	
	Yevgeny Valenrod	1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *20-23* is/are withdrawn from consideration.

5)☒ Claim(s) *11* is/are allowed.

6)☒ Claim(s) *1-10,12-19,24 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/20/06; 4/14/05; 1/18/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of N-[4-(tert-butyl)benzyl]-5{[(4-methylphenyl)sulfonyl]oxy}naphthalene-1-sulfonamide as a single species in the reply filed on 1/19/07 is acknowledged. The traversal is on the ground(s) that the requirement for specie election does not set forth an appropriate basis for finding lack of unity of invention. This is not found persuasive because PCT Rule 13.1 and PCT Rule 13.2 are discussed in the restriction requirement on page 3, 3rd paragraph. Lack of special technical feature that makes over the prior art was sited reason for finding lack of unity.

The requirement is still deemed proper and is therefore made FINAL.

Newly added claims 14-19, 24 and 25 are within the scope of the elected invention and are considered below.

Newly submitted claims 20-23 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claims 20-23 are directed towards a method of enhancing an effect of a cancer therapy and method of reducing side effect resulting from cancer therapy. The common technical feature between the method claims and the medicament/compound claims is the compound of formula (I). Compound of formula I has been disclosed by McKenzie et al. in (US 5707985) and therefore fails to be a special common technical feature that makes over the prior art.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 20-23 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Potential Rejoinder

2. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the

above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Claim rejections

3. No prior art that would anticipate or render obvious the elected species has been uncovered. The search has been expanded to include other additional claimed compounds that fall within the scope of the generic formula (I).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-9 and 12-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1 and 12 recite the following: "...selected from the group consisting of a compound represented by the following general formula (I) and a pharmacologically acceptable salt thereof, and a hydrate thereof and a solvate thereof...". It is unclear if the presented list is a list of alternatives or if combinations of the described ingredients are to be present in the medicament.

For purposes of advancing the examination, the examiner will read the limitation of claim 1 as: "...selected from the group consisting of a compound represented by the following general formula (I), pharmacologically acceptable salt thereof, hydrate thereof or a solvate thereof...".

5. Claims 1-10 12-19 and 24-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim one recites a limitation that excludes a compound of the presented formula and also: "...wherein each of A, Z, **R^5 and R^5** has the same meaning as that defined above is excluded". The above limitation excludes the definitions of the variables defined above and fails to provide any alternative definitions. In order to advance the prosecution of the application examiner will not interpret the above limitation to exclude the definitions of the variable substituents of formula (I). In addition, the same limitation repeats R^5 twice (see highlighted portion).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-9 and 12-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for enhancing the reduction in the survival rate of Jurkat cells when the compounds of the instant invention are administered with bleomycin (page 116 in the specification), does not reasonably provide enablement for treating any cancer. The specification does not enable any physician skilled in the art of medicine, to make the invention commensurate in scope with these claims. The how to make requirement of the enablement statute, when applied to process claims, refers to operability and how to make the claimed process work. "The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims", In re Rainer, 146 USPQ 218 (1965); In re Colianni, 195 USPQ 150, Ex parte Formal, 230 USPQ 546. The main issues are the correlation between clinical efficacy for cancer treatment and Applicants' Jurkat cell assay.

a) Determining if any particular claimed compound would treat any particular cancer would require synthesis of the compound, formulation into a suitable dosage form, and subjecting it clinical trials with a number of fundamentally different cancerous cell lines, or to testing them in an assay known to be correlated to clinical efficacy of such treatment. This is a large quantity of experimentation.

b) The direction concerning treating cancer is found in the specification on page 89, third paragraph and page 118, which merely states Applicants' intention to do so.

Doses required to practice their invention are not described in the specification. No range of doses is recommended. Since compound of the instant has ever been used to treat any cancer, how is the skilled physician to know what dose to use for each of the different types of cancers? Are the identical doses to be used for treating any cancer? There is an Jurkat cell proliferation assay described in the specification on page 116. Only relative data describing the effect of the compounds of the instant invention on one specific cell line (Jurkat) when administered to together with one cancer treatment agent (bleomycin)

c) There is no working example of treatment of any disease in man or animals. The Jurkat cell assay provides evidence that the present compounds enhance in vitro activity of bleomycin. However, enhancing *in vitro* activity of one specific agent in a specific cell line does not provide enablement enhancing *in vivo* activity of any cancer therapy in any type of cancer. Thus there are no working examples of providing cancer treatment to any human or any mammal

d) The nature of the invention is clinical treatment of cancer with via administering the compounds of formula (I) together with a known cancer treatment.

e) The skilled artisan would view cancer as a group of maladies not treatable with one medicament or therapeutic regimen. No single chemotherapeutic drug is useful for the treatment of every case of cancer. Indeed, some types of cancer to not respond well to any known chemotherapeutic drugs. According to the Merck Manual of Diagnosis and Therapy (Reference included with PTO-892), Hepatocellular carcinomas and renal cell carcinomas are not generally improved by chemotherapy. Acute

lymphoblastic leukemia, on the other hand, responds well to a number of drugs, including vincristine, anthracyclines, and aspariginases, while acute mylogenous leukemia, on the other hand, responds to fewer drugs and is usually treated with cytarabine in combination with daunorubicin or idarubicin. Breast cancer is best treated with surgery and/or radiation, but the prognosis can be improved by the addition of adjuvant chemotherapy.

It is well known in the art that certain drugs are used to treat certain cancers, and one skilled in the art would be able to, when confronted with a particular tumor, determine which existing drugs are likely to be useful for treating that tumor. However, it has not been fully determined which tumors will and will not respond to the treatment with the instantly claimed compounds in combination with various other therapeutic methods.

f) The artisan using Applicants invention would be a physician with a MD degree and several years of experience.

g) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See In re Fisher, 166 USPQ 18, at 24 (In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.), Nationwide Chemical Corporation, et al. v. Wright, et al., 192 USPQ 95 (one skilled in chemical and biological arts cannot always reasonably predict how different chemical compounds and elements might

behave under varying circumstances), Ex parte Sudilovsky 21 USPQ2d 1702 (Appellant's invention concerns pharmaceutical activity. Because there is no evidence of record of analogous activity for similar compounds, the art is relatively unpredictable) In re Wright 27 USPQ2d 1510 (the physiological activity of RNA viruses was sufficiently unpredictable that success in developing specific avian recombinant virus vaccine was uncertain).

h) The scope of the claims involves all of the thousands of compounds of claim 1 as well as the numerous diseases embraced by the term cancer. Thus, the scope of claims is very broad.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

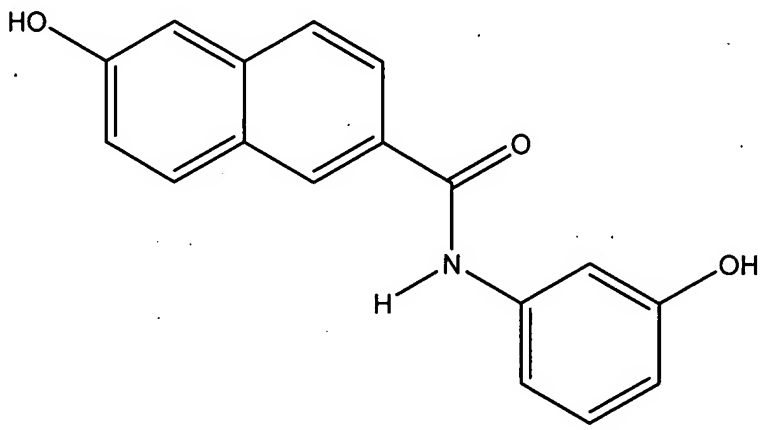
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 2, 6-10, 12, 13, 17, 24 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Marsilje et al (*Bioorganic & Medicinal Chemistry Letters* **2000**, *10*, pp477-481). Marsilje et al. disclose compound **2v** on page 478. Said compound the following structure:



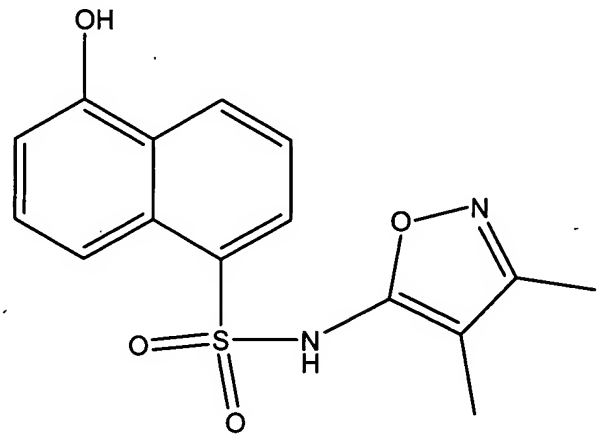
The above structure corresponds to compounds of the instant invention as follows:

R1 = H; R2 = OH; R3 = H; Y = CO; R6 = H; Z = bond; R5 = *m*-hydroxyphenyl. The structural limitations of the claims directed to compounds (claims 10, 24 and 25) and of the claims directed to a medicament (1, 2, 6-9, 12, 13 and 17) are met by compound **2v**.

Limitations of claims 1, 2, 6-9, 12, 13 and 17 that are directed to enhancing the effect of cancer treatment recite an intended use and are not considered as further limiting.

"It is well settled that the intended use of a composition or product (e.g. as a cosmetic composition) will not further limit claims drawn to a composition or product, so long as the prior art discloses the same composition comprising the same ingredients in an effective amount as instantly claimed" See, e.g., *Ex parte Masham,* 2 USPQ2d, 1647.

8. Claims 1, 2, 4-10, 12, 13, 15, 16, 24 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Stein et al (*J. Med. Chem.* **1995**, *38*, 1344-1354). On page 1347, Stein et al. disclose compound **71**:



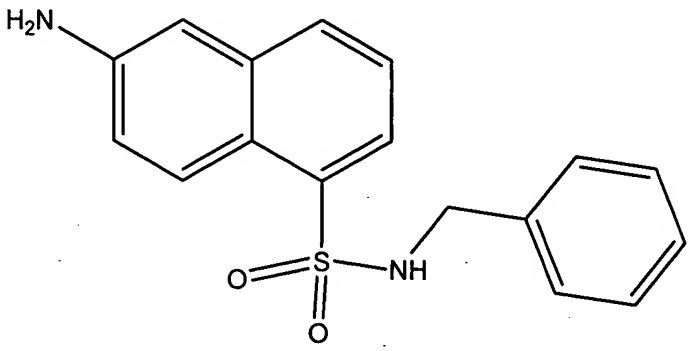
The above structure corresponds to the instantly claimed compounds as follows:

R1 = OH; R2 = J_2; Y = SO_2; Z = bond; R5 = substituted aromatic; R6 = H.

Compound 71 meets the structural limitations of claims 1, 2, 4-10, 12, 13, 15, 16, 24 and 25. Claims that are directed to a medicament are treated as claims with an intended use for the compound and the intended use is not given patentable weight.

"It is well settled that the intended use of a composition or product (e.g. as a cosmetic composition) will not further limit claims drawn to a composition or product, so long as the prior art discloses the same composition comprising the same ingredients in an effective amount as instantly claimed" See, e.g., *Ex parte Masham,* 2 USPQ2d, 1647.

9. Claims 1-4, 6-10, 12-15, 24 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Butenas et al. (*Biochemistry* **1992**, *31*, 5399-5411; CAS abstract is attached). Butenas et al. disclose a compound of the following formula:



The above compound meets the structural limitations of claims 1-4, 6-10, 12-15, 24 and 25. The variable groups correspond as follows:

R1 = H; R2 = NH_2 ; R4 = H; Y = SO_2; Z = CH_2; R6 = H; R5 = Phenyl.

Claims that are directed to a medicament are treated as claims with an intended use for the compound and the intended use is not given patentable weight.

"It is well settled that the intended use of a composition or product (e.g. as a cosmetic composition) will not further limit claims drawn to a composition or product, so long as the prior art discloses the same composition comprising the same ingredients in an effective amount as instantly claimed" See, e.g., *Ex parte Masham,* 2 USPQ2d, 1647.

Allowable subject matter

The specific compounds listed in claim 11 are neither anticipated nor suggested by prior art. The compounds have a disclosed utility of enhancing the effect of bleomycin in preventing differentiation of Jurkat cells. Stein et al., Marsilje et al. and Butenas et al. (cited above). Closest is Butenas et al., which differs from the compounds of the instant invention in that Butenas fails to disclose compounds where the N-benzyl substituent is substituted with the specific groups found in the compounds of claim 11. Also Butenas discloses a compound where R2 = NH_2 and therefore does not anticipate the compounds where R1 or R2 is a hydroxyl or a substituted oxygen. Midifying the compound disclosed by Butenas in such way as to obtain the compounds of the instant claim 11 lacks motivation.

Conclusion

Claims 1-25 are pending.

Claims 20-23 are withdrawn.

Claims 1-10, 12-19 and 24-25 are rejected.

Claim 11 is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yevgeny Valenrod whose telephone number is 571-272-9049. The examiner can normally be reached on 8:30am-5:00pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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